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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/820,599	04/08/2004	Balaraman Kalyanaraman	650053.00044	8142

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EXAMINER

LEARY, LOUISE N

ART UNIT	PAPER NUMBER
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1655

DATE MAILED: 01/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/820,599

Applicant(s)

KALYANARAMAN ET AL.

Examiner

Louise N. Leary

Art Unit

1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-25 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-25 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>1/19/2005</u> . | 6) <input type="checkbox"/> Other: ____. |

Art Unit: 1655

1. Claims 1-25 are pending in this application.
2. Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-5 are indefinite because it is unclear if the 2-hydroxyethidium compounds claimed occur in nature or are compounds ---isolated--- by a manmade process. It is suggested that ---isolated--- be added to clarify the subject matter claimed.

Claims 6-7 and 9-10 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: a description of the detection protocol or means.

Correction is required to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Art Unit: 1655

Claims 1-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Heryln et al (US 20020081711 June 27, 2002).

Heryln et al disclose 2-hydroxyethidium {HE}. Heryln et al disclose 2-hydroxyethidium {HE } is a fluorescent red dye. See page 23, section 0177.

Regarding the instantly claimed purity limitations for 2-hydroxyethidium, the examiner notes that determination of various degrees of purity of the 2-hydroxyethidium compound does not constitute patentable subject matter. The chemical structure for the 2-hydroxyethidium compound claimed is identical irrespective of the degree of purity.

4. (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-25 are rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Zhao et al (PNAS, V. 102(6), pp 1359-1368 (2003)).

Zhao et al disclose a method for detecting superoxide in a sample comprising the steps of adding hydroethidine to a cell sample containing superoxide to produce a fluorescent product. With respect to the limitations in instant claims 6-7, Zhao et al disclose "[In the present study, we show that superoxide generated in several

Art Unit: 1655

enzymatic or chemical systems (e.g., xanthine/xanthine oxidase, endothelial nitric oxide synthase, or potassium superoxide) oxidizes HE to a fluorescent product (excitation, 480 nm; emission, 567 nm) that is totally different from E+.]” See the abstract. In regards to instant claim 8 and instant claim 12, Zhao et al disclose “[HPLC measurements revealed that the HE/superoxide reaction product elutes differently from E+. Mass spectral data indicated that the molecular weight of the HE/superoxide reaction product is 330, while ethidium has a molecular weight of 314.]” See the abstract. Regarding the limitations of instant claim 13 which mixes “Fremy’s salt with HE and phosphate buffer to produce 2-hydroethidium, Zhao et al disclose isolating and characterizing a fluorescent product before this invention that is identical to the reaction product claimed. In regards to the limitations recited in instant claim 23, Zhao et al disclose using a silica gel column and chloroform elution of the desired reaction product(s). See page 1361. With respect to the limitations of instant claim 24 and instant claim 25, Zhao et al disclose or suggest separating and purifying the desired reaction product. Thus, Zhao et al disclose or suggest the invention claimed except for stating “2-dihydroxyethidium”.

However, regarding naming the reaction product “2-dihydroxyethidium” in the present invention, it is noted that Zhao et al disclose or suggest method steps and reactants claimed for inherently producing “2-dihydroxyethidium” as a reaction product. Also, it is noted that producing a known chemical product by a materially different method does not necessarily constitute patentable subject matter because the products recovered have identical chemical structures. Zhao et al disclose all the limitations

Art Unit: 1655

claimed in the present invention except for naming the reaction product "2-dihydroxyethidium inherently produced by the Zhao et al methods which anticipates or renders obvious the invention claimed.

The burden of proof is on applicants to show patentably distinct differences between the Zhao et al disclosure and the invention as presently claimed.

5. No claim is allowed.

6. The (PNAS, V. 102(6), pp5727-5732 (2005) reference and Zielonka et al (Free Radical Bio. Medicine, V. 19(7), pp 853-863 (10/2005) reference have been cited to further show the state of this art.

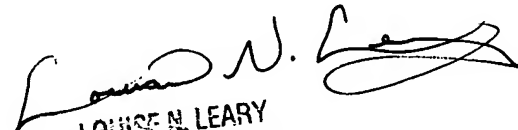
The Budd et al reference (FEBS Letters, V. 415, pp 21-24(1997) reacts cells with hydroethidine that is oxidized to fluorescent ethidium cation by O₂ whereby the reaction appears to yield a quantity of unrecovered product and has been cited to further show the state of this art.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise N. Leary whose telephone number is 571-272-0966. The examiner can normally be reached on Monday to Friday from 10 to 6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey, can be reached on 571-272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1655

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



LOUISE N. LEARY
PRIMARY EXAMINER

December 6, 2005